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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,418	12/22/2004	Guo-Wei Qin	SERVIER 438 PCT	7544

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,418	QIN ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19-29* is/are allowed.

6)☒ Claim(s) *30 and 32-35* is/are rejected.

7)☒ Claim(s) *31,33,34 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 27-38 are pending in the instant application.

Information Disclosure Statement

2. Applicants' Information Disclosure Statement (IDS), filed December 22, 2004, has been considered by the Examiner. Please refer to the signed copy of Applicants' PTO-1449 form, submitted herewith.

Response to Amendment

3. Applicants' Preliminary Amendment of December 2004, has been reviewed by the Examiner and entered in the file. Accordingly, claims 1-18 have been cancelled, and new claims 19-36 have been added.

Claim Rejections - 35 USC § 112

4. Claims 30 and 32-35 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. The specification, while being enabling for treating certain diseases that benefit from facilitating mnemocognition, does not reasonably provide enablement for treating all of the diseases/disorders encompassed by claims 30 and 32-35. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Regarding claims 30 and 32, the claims are not enabled for *any* and *all* neurodegenerative diseases or Alzheimer's.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The specification, while being enabling for compounds according to formula (I) for treating certain ageing diseases that respond to facilitating the central nervous system, does not reasonably provide enablement for treating all of the diseases encompassed by the above claims.

The nature of the invention

The nature of the invention is methods of treating inflammatory, immune, and proliferative disorders/diseases, or diseases involving the DHODH pathways, comprising administering a compound to a patient in need thereof. The language of claims 36-38 encompasses *any* or *all* neurodegenerative disorders, including Alzheimer's.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is

highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of all diseases, whether or not the disease is affected by the inhibition of cellular levels of IL-8 or GRO-α would make a difference.

It is the state of the art that there is no known cure or prevention for Alzheimer's disease, furthermore, there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, ARICEPT®, EXELON®, REMINYL® and COGNEX®, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. MEMANTINE®, which blocks excess amounts of glutamate, treats late stage Alzheimer's disease. (URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html).

Hence, in the absence of a showing of the ability of the instant claimed compounds to treat all of the diseases claimed by facilitating the central cholinergic system and since the treatment of Alzheimer's disease is mediated by the breakdown of acetylcholine or the inhibition of excess amounts of glutamate, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula (I) due to the unpredictability of neurodegenerative diseases.

The amount of direction or guidance present and

the presence or absence of working examples

The specification also only discusses three murine assays on pages 20-22 which demonstrate the instant compounds' anti-amneisc effects on mice and rats, and provides no data for describing the efficacy of the claimed compounds for treating the full scope of disorders that Applicants have claimed. On page 1 of the specification, Applicants report that "[t]he majority of

substances used today in treating cognitive disorders associated with ageing act by faciliting the central cholinergic systems..." yet there is no correlation shown between the central cholinergic system, Alzheimer's disease, and the compounds of the instant invention, i.e. the specification is silent as to the claimed compounds' efficacy for treating any neurodegenerative diseases *in vivo*.

The breadth of the claims and the quantity of experimentation needed

The breadth of the claims is the treatment of all diseases of claims 30 and 32, including Alzheimer's disease. The quantity of experimentation needed is undue experimentation. Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the art would be burdened with undue "experimentation study" to determine whether the claimed compounds not only facilitate the central cholinergic system, but have efficacy for treating Alzheimer's disease, of which there is no known cure.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test whether Alzheimer's disease can be treated by the compound encompassed in the instant claims, with no assurance of success.

Regarding claims 30 and 32, the Examiner suggests narrowing the scope of the possible diseases and conditions that are treated to those that Applicants can provide enabling support for.

Double Patenting

5. Claim 34 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 33. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objections

6. Claims 31 and 36 are composition claims drafted in terms of intended use. The Examiner would like to remind Applicants that the preambles recite pharmaceutical compositions, and while the use of a descriptive clause, i.e. "for the treatment of...," when referring to the contemplated use (i.e. "intended use") of a claimed compound is proper, it is not a limitation and thus of no significance in determining the patentability thereof over the prior art, please refer to *In re Thomas (CCPA 1949) 178 F2d 412, 84 USPQ 132.* Therefore, composition claims 31 and 36 are duplicates.

Conclusion

7. In conclusion, claims 19-36 are pending, claims 30 and 32-35 stand rejected, and claims 31, 33, 34, and 36 are also objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Coppins
April 2, 2007

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

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